Citation:

Patel AV, McCullough ML, Pavluck AL, Jacobs EJ, Thun MJ, Calle EE. Glycemic load, glycemic index, and carbohydrate intake in relation to pancreatic cancer risk in a large US cohort. *Cancer Causes Control*. 2007 Apr; 18(3): 287-294. Epub 2007 Jan 11.

PubMed ID: 17219014

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the association between glycemic load (GL), glycemic index (GI), carbohydrate intake and pancreatic cancer risk among men and women in the American Cancer Society Cancer Prevention Study II (CPS-II) Nutrition Cohort, a large prospective study in the US.

Inclusion Criteria:

Men and women in this analysis were drawn from the 184,190 participants in the CPS-II Nutrition Cohort, which was established in 1992 by the American Cancer Society as a subgroup of the larger 1982 CPS-II base-line mortality cohort.

Exclusion Criteria:

- Individuals who died from any cause within the first year of follow-up to reduce the possibility of undiagnosed disease at baseline (N=741), and those with an unverified date of diagnosis of pancreatic cancer (N=2)
- Participants who reported prevalent cancer (except non-melanoma skin cancer) at baseline (N=21,026), who left 10 or more of the 68 questions (15% of items) on the dietary section of the 1992 questionnaire blank (N=11,835) or who had extreme values of daily energy intake (i.e., less than 500 or more than 3,500kcals for women and less than 650 or more than 4,000kcals for men) (N=3,028) or body mass index (BMI) (N=4,152) and individuals who had missing information on smoking status (N = 1,231)
- Individuals who reported a personal history of diabetes at baseline (N=10,265). Individuals who did not return a 1999 or 2001 questionnaire were censored at the 1997 questionnaire date. Individuals were also were censored at report of diabetes on the 1997 or 1999 questionnaire.

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Description of Study Protocol:

Recruitment

Men and women in this analysis were drawn from the 184,190 participants in the CPS-II Nutrition Cohort, which was established in 1992 by the American Cancer Society as a subgroup of the larger 1982 CPS-II base-line mortality cohort.

Design

Prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

- Usual dietary intake over the past year was assessed at baseline using a semi-quantitative 68-item food-frequency questionnaire (FFQ) that was a modification of the brief ''Health Habits and History Questionnaire'' developed by Block et al. Daily nutrient intake was estimated from the FFQ using the ''Health Habits and History Questionnaire'' diet analysis software DIETSYS, Version 3.8a
- Median validity and reproducibility correlations for nutrients and food groups on the FFQ were 0.58 and 0.69, respectively
- Reproducibility correlations for carbohydrate intake specifically were 0.73 for men and 0.51 for women
- Total daily dietary glycemic load and GI values were derived from food intake reported on the FFQ. The GI value of a specific food represents a ratio measure for the incremental increase in blood glucose after its consumption relative to that induced by a standard food, white bread
- Glycemic index values for individual food items were added to the nutrient database using published data of glycemic responses measured using standardized analytic methods
- In the case of multiple line items (i.e., multiple food items listed together) on the Block FFQ, the GI for each food was estimated and assigned the line item the weighted average of GI values based on the prevalence of consumption of these items in the population
- The glycemic load of the total diet was calculated by summing across all food items the products of:
    - GI for that food
    - Grams of carbohydrate per serving of that food
    - Number of daily servings
- To derive a score for total dietary GI, the dietary glycemic load of the total diet was divided by the total dietary carbohydrate intake in grams
- Dietary glycemic load and index were evaluated to examine a quantitative measure of the glucose response induced by total daily carbohydrate intake and a score reflecting the relative proportion of high GI foods composing the diet, respectively
- To control for energy intake, measures of dietary GI and load, and carbohydrate intake were adjusted for total energy using the residuals method.

Statistical Analysis

- Cox proportional hazards modeling was used to calculate hazard rate ratios (RR) and corresponding 95% confidence intervals (CI) to examine the relationship between sex-specific quintiles of glycemic load, GI and carbohydrate intake and pancreatic cancer
- For each exposure variable, risk was assessed in two models, one adjusted for age and sex and the other adjusted for age, sex and potential confounding factors

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- All Cox models were stratified on exact year of age at enrollment
- Other risk factors or potential confounders included in the multivariate models were smoking status (never, current, former) and time since quitting for former smokers (less than 10, 10–19 and more than 20 years), race (white, non-white),BMI (weight in kg/m^2) (less than 25.0, 25.0 to less than 30.0, more than 30.0) location of weight gain (central, peripheral, other or unknown), and sedentary behavior (less than three hours per day, three to five hours per day or six or more hours per day spent sitting). Sedentary behavior was used as a measure of inactivity instead of MET-hours per week of recreational activities because sedentary behavior, not physical activity, predicted for pancreatic cancer in this cohort. Adjustments were made for personal history of gallbladder disease (yes, no), first-degree family history of pancreatic cancer (yes, no), total caloric intake (quartiles) and sex (male, female). Total intake of fat and protein were also examined as potential confounders but were not included in the final models because such adjustment had negligible effects on the results (data not shown)
- Trend tests for all exposure variables were conducted by constructing a continuous trend variable that assigned the sex-specific median values within each quintile category to that category.

Data Collection Summary:

Timing of Measurements

- This analysis is based on nine years of follow-up
- Nearly all participants were 50 to 74 years of age at enrollment in 1992 when they completed a ten-page self-administered questionnaire that included questions on demographic, medical and dietary factors
- Beginning in 1997, follow-up questionnaires were sent to cohort members every two years to update exposure information and to ascertain newly diagnosed cancers. Follow-up questionnaire response rates among living cohort members have been at least 90%. Cohort members who died are identified by routine linkage of the entire cohort with the National Death Index (NDI).

Dependent Variables

Pancreatic cancer risk.

Independent Variables

- Glycemic load
- Glycemic index
- Intake of carbohydrates
- Control variables.

Description of Actual Data Sample:

- *Initial N:* 184,190
- *Attrition (final N):* 124,907
- *Mean age:* At study entry 62.7 years (+ 6.35 SD)
- *Location:* US.

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Summary of Results:

- No association between GL, GI or carbohydrate intake and risk of pancreatic cancer in this population
- No significant association between these measures and pancreatic cancer risk among individuals who show greater susceptibility to insulin resistance.

Author Conclusion:

Study findings do not support the hypothesis that glycemic load or index, or carbohydrate intake are associated with a a substantial increase in pancreatic cancer risk. However, there may be a weak positive association.

Reviewer Comments:

None.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes

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2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	N/A
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	???

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5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	???
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	N/A
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	N/A
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	N/A
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	N/A
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	N/A
7.6.	Were other factors accounted for (measured) that could affect outcomes?	N/A

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	7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	N/A
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	No
	10.2.	Was the study free from apparent conflict of interest?	???

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